

### REMARKS

The present claims concern methods for detecting intracellular analytes using flow cytometry, by using enzyme catalyzed tyramide deposition, such that at least a 10-fold enhancement in specific signal is obtained over standard flow cytometry methods.

Applicant appreciates the Examiner's indication that claims 6-9 and 20-22 would be allowable if rewritten to incorporate all the limitations of the base claim and any intervening claims.

Applicant also appreciates the helpful telephonic interview with the Examiner and Supervisor Long Le on March 11, 2004, and the follow-up discussions with the Examiner on March 12, March 16, and March 17, 2004. As the Examiner agreed in the discussions on March 16 & 17, 2004, claims 1 and 2 as amended above are distinguished over the references cited by the Examiner in the outstanding Office Action.

Thus, Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Claims 1 and 2 are currently being amended, and new claims 62-66 are being added. Support for limitation in claim 1 is provided in the specification, for example, at p.17, line 35 to p.18, line 8. Similarly, support for new claims 62-66 is provided in the specification, inter alia, at p.18, lines 1-8. Thus, the amendments to the claims do not add any new matter.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

After amending the claims as set forth above, claims 1-33 and 62-66 are now pending in this application.

Rejections under 35 U.S.C. § 103

The Examiner rejected claims 1-5, 10, 14-18, 25-26, and 28-30 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Karkmann et al. (J. Immu. Methods. 1999) in view of Koester et al. (J. Immunol. Methods, 2000, 243:99-106), and rejected claims 1-5, 11-19, and 23-33 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Lollini et al. (Immunological Blackboard, 1998) in view of Koester et al. The Examiner stated that Karkmann et al. and Lollini et al. describe tyramide-based signal amplification methods. Applicant respectfully traverses these rejections as they may be considered in connection with the amended claims.

As was discussed with the Examiner during the telephonic interview on March 11, 2004, the present claimed methods are distinct from the methods described in Karkmann et al. and Lollini et al. because the present methods provide at least 10-fold enhancement in specific signal, while neither of those reference provide such enhancement. In particular, this distinction was discussed in the Declaration of Dr. David R. Kaplan filed October 16, 2002.

In addition, the present methods are distinct from those described in Karkmann et al. and Lollini et al. by using agents (e.g., elevated concentrations of protein) that are much more effective in reducing non-specific binding than the 0.5% BSA or 1.0% BSA utilized in the Karkmann et al. and Lollini et al. methods respectively (i.e., reducing non-specific binding at least as much as the presence of 10% fetal bovine serum). Neither Karkmann et al. nor Lollini et al. suggest using such high protein concentration or any other agent similarly effective in reducing non-specific binding.

Further, the Examiner requested that Applicant submit a Declaration showing that the present methods provide the specified 10-fold signal enhancement with 10% serum. In response,

Applicant submits herewith a second Declaration of Dr. David R. Kaplan. As shown by the results summarized therein, the present methods provide at least a 10-fold enhancement when 10% serum is used as specified in claims 1 and 2.

Thus, in view of the discussion above, the Amendment, and the Declaration of Dr. David R. Kaplan filed herewith, Applicant respectfully submits that none of the references cited by the Examiner, either alone or in combination make the present claims obvious. Therefore, Applicant requests that the Examiner reconsider and withdraw the rejections under 35 U.S.C. § 103.

Favorable reconsideration of the application as amended is respectfully requested. Applicant respectfully submits that that the present application is now in condition for allowance, and requests a notice to that effect.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-0872. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-0872. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 50-0872.

In re Application of  
David R. Kaplan  
Application No. 08/738,049

Atty. Dkt. No. 071957-0903

Respectfully submitted,

Date 23 March 2004

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